REMARKS/ARGUMENTS

Claim Status/Support For Claim Amendments

In response to the Office Action of March 11,2003, Applicants request re-examination and reconsideration of this application for patent pursuant to 35 U.S.C. 132.

Claim 1 has been amended. Claims 2-35 have been canceled. Claims 36-43 have been added. Claims 1 and 36-43 are pending in the instant application.

No new matter has been added by the addition of new claims 36-43. The subject matter of new claims 36-43 corresponds to the subject matter of canceled claims 3-28. The above additions to the claims also find basis in the original disclosure at page 12, lines 2-12; page 17, lines 7-14; page 18, lines 5-7 and page 27, line 17 to page 28, line 2. The method of claims 36-40 is described in detail at pages 20-27. Page 28,line 11 to page 29,line 7 refers to the use of various types of samples and their measurement. Figure 1 shows data derived when using the claimed method on samples obtained from a human patient. Page 28, line 3 to page 33, line 2 describes kits and their contents contemplated for use with the claimed methods. It is clear from these specific recitations and from the description of methods utilized that the methods and types of kits were fully contemplated by the inventors at the time of filing and were enabled by virtue of the disclosure as originally

filed.

Considering that new claims 36-43 are limited to the use of a peptide consisting of amino acid residues 2-17 of SEQ ID NO:1, a search of these claims would encompass this specific peptide. As was mentioned in the Response filed on December 30,2002, the instant application is related, in claim format, to several other pending applications. In an effort to maintain equivalent scope in these applications, Applicants would appreciate the Examiner's reconsideration of the restriction requirement in light of the overlapping search and rejoin under *Ochai* claim 1 which is drawn to a specific peptide to claims 36-43 which are drawn to methods and kits limited to use of the specific peptide of claim 1.

Sequence Compliance

Applicants have reviewed the entire specification including the figures and the claims for sequence disclosures. The only sequence found to be disclosed is the amino acid sequence identified as SEQ ID NO:1. Applicants provided a Sequence Listing (in both paper and computer readable form) disclosing SEQ ID NO:1 on April 19, 2002. However, Applicants noted that amino acid residue 1 of SEQ ID NO:1 as shown in Figure 2 was not included in the originally filed Sequence Listing. Applicants herein provide a diskette containing a substitute Sequence Listing in electronic computer readable form to replace the previously submitted copy

(filed on April 19, 2002). The diskette submitted herewith contains a Sequence Listing which adds amino acid residue 1 to SEQ ID NO:1. As shown in Figure 1, the marker identified in patient sera consists of amino acid residues 2-17 of SEQ ID NO:1. When carrying out mass spectrometric procedures, it is possible to fragment a whole molecule, depending upon the enzyme used for digestion. A sequence is often predicted from these fragments but often the sequence is not identified completely. It is conventional in the art to show the missing portions of the predicted sequence in parentheses. The first and last amino acid residues of SEQ ID NO:1 are predicted residues as indicated by the parentheses in Figure 1. The peptide sequence without amino acid residue 1 was shown in the original specification at page 27, line 18 and is shown in Figure 2 with amino acid residue 1. Thus, no new matter is added, the substitute Sequence Listing is for the purpose of clarifying the use of parentheses only. Applicants also herein provide a substitute paper copy of the Sequence Listing as contained on the diskette filed herewith. The computer readable form of the substitute Sequence Listing is identical to the paper copy of the substitute Sequence Listing. The amendments to the claims and specification limiting the marker sequences to specific amino acid residues are also made for the purpose of clarification only. The claims as herein amended limit the marker sequence to amino acid residues 2-17 of SEQ ID NO:1.

Rejections under 35 USC 112 (second paragraph)

Claims 3-28, as originally presented, stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner alleges that claims 3,4 and 5 are vague and indefinite in reciting the term "evidencing" because it is unclear what Applicant intends to encompass in such a recitation. Claims 3-5 have been canceled and the term "evidencing" is not recited in any of the remaining pending claims.

The Examiner alleges that claims 3, 4, 10, 18 and 25 are vague and indefinite in reciting the phrase "biopolymer marker sequence or analyte thereof" because it is unclear how an element is an analyte of a biopolymer marker. Claims 3, 4, 10, 18 and 25 have been canceled and the phrase "analyte thereof" is not recited in any of the remaining pending claims. It is noted that on page 4 of the Office Action mailed March 11, 2003, in the first rejection of claim 10, there is an unfinished sentence "See also claim". Is this a typographical error or were other claims meant to be included with this rejection?

Additionally, the Examiner alleges in claim 3 that the phrase "biopolymer marker sequence or analyte thereof" lacks antecedent support because it is unclear how the biopolymer marker was isolated from the sample. Claim 3 has been canceled and the

phrase "biopolymer marker sequence or analyte thereof" is not recited in any of the remaining pending claims.

The Examiner alleges that it is unclear in claim 3 what property or element of the isolated biopolymer marker is compared to that of SEQ ID NO:1 in claim 1. Claim 3 has been canceled and corresponding new claim 36 has been amended to clearly indicate that the mass spectrum profile of the isolated biopolymer marker is compared to the mass spectrum profile of amino acid residues 2-17 of SEQ ID NO:1.

The Examiner alleges that claim 3 is ambiguous in reciting "wherein correlation of said isolated biopolymer marker and said biopolymer marker sequence as forth in claim 1 evidences and categorizes said at least one disease state" because it is unclear how these two elements are correlated so as to provide confirmation of the presence of a disease state. Claim 3 has been canceled and corresponding new claim 36 has been amended to clearly indicate that mass spectrometric profiles are compared so as to provide confirmation of a disease state.

The Examiner alleges that claims 4 and 5 are indefinite in reciting the term "particularly" because particularly is a subjective term that lacks a comparative basis for defining its metes and bounds. Claims 4 and 5 have been canceled and the term "particularly" is not recited in any of the remaining pending claims.

The Examiner alleges that claims 4 and 5 are confusing because it is unclear what functional cooperative relationship exists between the recitation of "directed to biopolymer markers or analytes thereof linked to at least one risk of disease development" and the "at least one isolated biopolymer marker sequence" (which is SEQ ID NO:1) recited in claim 3. The Examiner questions if there is more than one biopolymer marker sequence involved. Claims 4 and 5 have been canceled and the corresponding new claims have been amended to clearly indicate that there is one biopolymer marker sequence (which is a peptide consisting of amino acid residues 2-17 of SEQ ID NO:1)diagnostic for Type II diabetes involved in the methods and kits of the instant invention.

The Examiner alleges that claims 10 and 18 are indefinite in failing to recite a positive limitation in the claims in reciting "capable of". Claims 10 and 18 have been canceled and the phrase "capable of" is not recited in any of the remaining pending claims.

The Examiner alleges that claims 11 and 19 have improper antecedent basis in reciting "said biochemical material or biomolecule". Claims 11 and 19 have been canceled and the phrase "said biochemical material or biomolecule" is not recited in any of the remaining pending claims.

The Examiner alleges that claims 12 and 14 are vague and indefinite in relation to claim 10 in reciting "at least one labeled biochemical material" because it is unclear as to whether

the biochemical material in claims 12 and 14 is the same as the biochemical material recited in claim 10, but including a label. Claims 12 and 14 have been canceled and the phrase "at least one labeled biochemical material" is not recited in any of the remaining pending claims.

The Examiner alleges that the term "therefore" in claims 17 and 25 should be --therefor--. Claims 17 and 25 have been canceled and neither "therefore" nor --therefor-- is recited in any of the remaining pending claims.

The Examiner alleges that claim 18 is confusing in reciting "at least one analysis to determine a presence of..a biochemical material" because the assay kit appears to be drawn to its use in determining the presence of a biopolymer marker using the biochemical material, and not to determining the presence of the biochemical material, i.e. antibody specific thereto. Also with regard to claim 18, the Examiner alleges it is unclear what structural and functional cooperative relationship exists between "a biochemical material" (second occurrence in the claim) and "at least one biochemical material" (first occurrence in the claim). Claim 18 has been canceled and none of the phrases referred to above in the instant paragraph are recited in the remaining pending claims.

The Examiner alleges that claims 20 and 22 are vague and indefinite in relation to claim 18 in reciting "at least one

labeled biochemical material" because it is unclear as to whether the biochemical material in claims 20 and 22 is the same as the biochemical material recited in claim 18, but including a label. Claims 20 and 22 have been canceled and the phrase "at least one labeled biochemical material" is not recited in any of the remaining pending claims.

The Examiner alleges that claims 21 and 25 lack clear antecedent support in reciting "said biochemical material" since claim 18 appears to recite more than one biochemical material. Claims 21 and 25 have been cancelled and the phrase "said biochemical material" is not recited in any of the remaining pending claims.

The Examiner alleges that claims 26-28 are confusing because they depend from and are intended to be drawn to "an assay kit" but the limitations set forth in these claims appear to be drawn to a method. Claims 26-28 have been canceled and new claims 41-43 drawn to kits clearly recite a kit and the components of said kit and do not recite a method.

Accordingly, applicants have now clarified the metes and bounds of the claims and respectfully request that all of the above-discussed rejections be withdrawn.

Rejection under 35 USC 112 (first paragraph)

Claims 3-28, as originally presented, stand rejected under 35

U.S.C. 112, first paragraph, as containing subject matter which allegedly was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims as amended have been limited to a specific biopolymer marker peptide consisting of amino acid residues 2-17 of SEQ ID NO:1 (the 1998 dalton marker) useful in methods and kits for diagnosing Type II diabetes. The method of the invention as recited in claim 36 involves a comparison of the mass spectrum profile of a peptide consisting of amino acid residues 2-17 of SEQ ID NO:1 to mass spectrum profiles of peptides elucidated from a patient sample, wherein recognition of a mass spectrum profile in the patient sample displaying the characteristic profile of the mass spectrum of the peptide consisting of amino acid residues 2-17 of SEQ ID NO:1 indicates that the patient from which the sample was obtained is suffering from Type II diabetes. Each patient listed in the data table shown in Figure 1 has a history of Type II diabetes and shows the presence of the 1998 dalton marker (amino acid residues 2-17 of SEQ ID NO:1) in their serum.

Applicants herein provide the attached Declaration (and figure) under 37 CFR 1.132 in order to establish the specificity of the claimed marker. The profiles shown in the figure attached to the declaration indicate that the claimed method can be used to

distinguish individuals suffering from Type II diabetes from those not inflicted with Type II diabetes. The figure attached to the declaration provides side-by-side profiles (obtained using techniques of mass spectrometry) of normal human sera versus sera from patients having Type II diabetes. This profile comparison clearly evidences the absence of the 1998 dalton marker in normal human sera and thus establishes the specificity of the 1998 dalton peptide as a marker which when present in the sera is diagnostic for Type II diabetes.

Applicants now submit that one of skill in the art would know how to use the claimed methods and kits to diagnose Type II diabetes in an individual and respectfully request that this rejection be withdrawn.

Rejection Under 35 USC 103(a)

Claims 3-28, as originally presented, stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Hutchens *et al.* (US 6,225,047) in view of Capiaumont *et al.* (Clinica Chimica Acta 293:89-103 2000).

Hutchens *et al.* teach a method for identification of analytes that are differentially present between two samples using retentate chromatography and desorption spectrometry. Hutchens *et al.* do not identify SEQ ID NO:1 of the instant invention with the use of their methods.

Capiaumont *et al.* is deemed to teach SEQ ID NO:1 which is C3F; a fragment of human complement containing the HWESAS motif which evidences chronic renal failure. Capiaumont *et al.* is recognized to teach a method for detection of the HWESAS hexapeptide in serum using an ELISA assay. Through use of their assay, Capiaumont *et al.* discover that patients with chronic renal failure exhibit an undetectable concentration of hexapeptide HWESAS and suggest that this hexapeptide could be used as a marker for renal function (see abstract and page 101 of Capiaumont *et al.*)

The Examiner states at page 14 of the Office Action mailed on March 11, 2003 that it would have been obvious to one of ordinary skill in the art at the time that the instant invention was made to combine Capiaumont's teaching of SEQ ID NO:1 as diagnostic of a disease state (chronic renal failure) with the method taught by Hutchens. It is noted that Capiaumont and Hutchens use entirely different techniques to identify peptides and neither suggests the use of alternative techniques. Additionally, Capiaumont *et al.* teach only six amino acid residues of SEQ ID NO:1 as a potential marker and do not teach the entire length of SEQ ID NO:1 as does the instant invention. Furthermore, the claims have been amended to limit the instant invention to a specific biopolymer marker peptide (amino acid residues 2-17 of SEQ ID NO:1; the 1998 dalton marker) diagnostic for Type II diabetes. Neither Capiaumont *et al.* nor Hutchens *et al.* teach or suggest that any part of SEQ ID NO:1

can be used as a diagnostic marker of Type II diabetes.

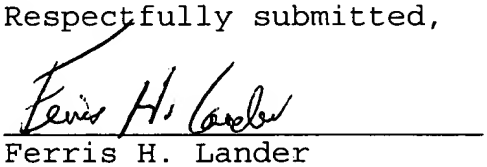
It is respectfully submitted that the ordinary skilled artisan, having both references in front of him/her (Capiaumont *et al.* and Hutchens *et al.*) would not be motivated to use retentate chromatography and desorption spectrometry to identify amino acid residues 2-17 of SEQ ID NO:1 as a marker diagnostic for Type II diabetes.

Thus, it is respectfully submitted that the combination of Hutchens *et al.* in view of Capiaumont *et al.* fails to reasonably teach or suggest to one of ordinary skill in the art the elements of the invention as specifically set forth in the instantly amended claims.

SUMMARY

In light of the foregoing remarks and amendments to the claims, it is respectfully submitted that the Examiner will now find the claims of the application allowable. Favorable reconsideration of the application is courteously requested.

Respectfully submitted,



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